IN THE CLAIMS:

Please cancel claims 2, 3, 6, 8-20, 15, 17-19, and 22-29 without prejudice.

Please amend claims 1, 7, and 21 as follows:

1. A method of stimulating an immune response against a tumor antigen in a mammal, the method comprising administering to said mammal said tumor antigen and a lactadherin or a polypeptide comprising a lactadherin amino acid sequence, said polypeptide comprising a functional integrin binding site of lactadherin represented by the RGD motif.

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7. The method of any one of claims 1-5, wherein said polypeptide is human lactadherin or a polypeptide comprising a functional integrin binding site of human lactadherin.

21. The method of claim 1, wherein said lactadherin has the amino acid sequence of SEQ ID NO: 2 or 4 or a part thereof comprising of a functional integrin binding site, said part comprising amino acid residues Arg Gly Asp at position 46-48 of SEQ ID NO: 2 or amino acid residues 87-89 or SEQ ID NO: 4.

SEQUENCE LISTING

Typographical errors in the sequence listings have been corrected. A substitute CRF and substitute paper copy are provided. Pursuant to 37 C.F.R. § 1.825, the computer-readable and paper form are the same and include no new matter.

§ 112 First Paragraph

The amended claims delete the previously pending reference to the lactadherin fragment. While many fragments of lactadherin are substantial equivalents of the claimed polypeptide, Applicant cannot foresee all of the possible sequences that could be synthesized and has, accordingly, recited a polypeptide comprising a lactadherin sequence.

The term "fragment" of claim 1 has been replaced with the expression "polypeptide comprising a lactadherin amino acid sequence" and the functional integrin binding site of lactadherin has been defined "the RGD motif." Such definition is clearly given in the application, in particular page 7, line 6, page 8, lines 17-18 and 22-23, and page 13, line, 2, for instance.

Also, claim 1 has been amended and is limited to a method of stimulating an immune response "against a tumor antigen" in a mammal.

Claim 7 has been adapted to claim 1.

Claims 2-3, 6, 8-15, 17-20 and 22-29 have been deleted.

Claim 21 has been amended. The term "fragment" has been replaced with the word "part" related to the functional integrin binding site, which "part" has been defined as

"comprising amino acid residues Arg Gly Asp at position 46-48 of SEQ ID NO:2 or amino acid residues 87-89 of SEQ ID NO:4."

Support for this amendment can be found for instance at page 8 (lines 19-21): "the integrin binding site of human lactadherin of SEQ ID NO:1 lies in residues 46-48 and the integrin binding site of murine lactadherin of SEQ ID NO:4 lies in residues 87-89." PAge 27, lines 14-15 states that "[...] amino acid residues Arg Gly Asp [are] at position 46-18 of SEQ ID NO:1." Pages 26 (lines 31-33) and 27 (line 1) and the sequence listing further explain that the mature protein sequence is represented on SEQ ID NO:1 and also on SEQ ID NO:2.

These amendments thus find explicit support in the specification as filed, do not add any new matter, and entry thereof is respectfully requested.

§ 102(b)

Regarding the disclosure of USP 5,505,955 and the application to the pending claims under § 102(b), the recitation of claim 1 is as follows:

> 1. A method of stimulating an immune response against a tumor antigen in a mammal, the method comprising administering to said mammal said tumor antigen and a lactadherin or a polypeptide comprising a lactadherin amino acid sequence, said polypeptide comprising a functional integrin binding site of lactadherin represented by the RGD motif. (emphasis added)

Applicant claims a method that produces an immune response against a tumor antigen" and that the administration step includes both "said tumor antigen" and a "polypeptide comprising a functional integrin binding site of lactadherin..." Thus, the claimed invention includes the step of administering both the tumor antigen and the polypeptide containing the functional binding site of lactadherin. This element absolutely is not disclosed by the '955 USP

reference or the WO 95/15171 reference and the Examiner cannot maintain the rejection under 35 U.S.C. § 102(b) based on these references

USP 5,505,955 merely discloses the use of:

defatted human milk fat globule, the human milk macromolecular fraction, the human milk mucin-70 Kd apparent MW glycoprotein-46 Kd apparent MW HMFG glycoprotein complex, the 46 Kd apparent MW HMFG glycoprotein, a polypeptide comprising an amino acid sequence having the rotavirus-binding specificity of the 46 Kd apparent MW HMFG glycoprotein, or mixtures thereof to provide a non-immunological method for treating diarrhea. As such this reference cannot anticipate a claim reciting the administration of both the tumor antigen and the lactadherin polypeptide to stimulate an immune response.

The disclosure of the '955 patent is almost totally unrelated to the present invention. Nothing in the '955 patent expressly or inherently discloses the ability of lactadherin to interact with dendritic cells and to deliver antigens and the compositions used in the claimed method are not even contemplated. Therefore, the claims are not anticipated by USP 5,505,955 because neither reference discloses the step of administering the tumor antigen and the polypeptide comprising a lactadherin sequence. Absent such disclosure, the amended claims cannot be rendered invalid under 35 U.S.C. § 102.

The WO 95/15171 reference was addressed in Applicant's previous response and fails to anticipate the pending claims for the same reason. The reference discloses administration of a single polypeptide that is expressly stated to be "unlikely to elicit toxic, immunological or allergic reactions in treated subjects." Thus, stimulation of an immune response by administering a human antigen and lactadherin polypeptide is not disclosed.

The Examiner's continued citation to Application of Best, 562 F.2d 1252, 1255 (CCPA 1977) cannot cure the deficiency of the references. When a claim recites the stimulation of an immune response, a reference whose purpose is to avoid an immune response cannot be cited as inherently disclosing the immune response of the claims. An element that is expressly avoided by the reference is not inherently disclosed thereby for § 102 purposes.

Applicant submits that the claims are in condition for allowance and request such action accordingly.

Respectfully submitted,

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